



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,327	08/18/2000	Gregory E. Agoston	05213-0730 (43170-219693)	7032

23370 7590 12/02/2002

JOHN S. PRATT, ESQ
KILPATRICK STOCKTON, LLP
1100 PEACHTREE STREET
SUITE 2800
ATLANTA, GA 30309

EXAMINER

QAZI, SABIHA NAIM

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 12/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

*Continuation is filed
6/26/03.*

Office Action Summary

Application No.

09/641,327

Applicant(s)

AGOSTON ET AL.

Examiner

Sabiha Naim Qazi

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 09 September 2002 and 25 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 10-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 10-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8,17 + 9, 6) ☐ Other:

Art Unit: 1616

This application is drawn to method of treating angiogenesis by 2-substituted estradiols.

Amendments filed in paper no. 16 are entered. Claims 10-30 are pending. No claim is allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-30 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Following reasons apply.

1. In evaluating the enablement question, several factors are to be considered. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) The nature of the invention: Instant claims are drawn to the method of treating angiogenesis by 2-substituted estradiol derivatives of formula in claim 10 and 19.

2) The state of the prior art: Prior art of record teaches method of treatment of angiogenesis, for example 2-methoxy estradiol, 2-ethoxy estradiol, 2-alkoxyestradiol derivatives, esterone, 2-hydroxyalkylestradiols, 2-methoxyesterone-3-O-sulfamate. All the compounds are estradiol or esterone derivative known to treat angiogenesis or cancer.

Art Unit: 1616

3) The predictability in the art: There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). The unpredictability of the steroid art is very high. Applicants own disclosure can be taken as example for lack of predictability, on page 20 lines 20-25, it has been shown that 2-methylhydroxy and 2-formyl derivatives had good antiproliferative activity ($IC_{50} < 10 \mu M$) in HUVEC cells whereas 2-acetyl derivative was found with poor activity in the same assay. The difference in range is less than 10 to 18, which is large. Furthermore, 2-methylhydroxy and 2-formyl derivatives were inactive in breast tumor MDA-MB-231 cells while 2-acetyl estradiol had good activity in this cell line.

It should be clear from these results and discussion that to predict the activity of hundreds of compounds as instantly claimed seems to be impossible. See *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. *In re Dreshfield*, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F.2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F.2d 349, 151 USPQ 724. Therefore, predicting the activity of all the estradiol derivatives as in claims 10 and 19 is impossible.

4) The presence or absence of working examples:

On page 20, Table 1 shows the test data for the compounds 2-methylhydroxy-E2, 2-formyl-E2 and 2-acetyl-E2 (2ME2 is known), all these compounds are 2-substituted, others are hydrogen. There is no data for compounds having variety of substituents at 1, 2, 3, 4, 6, 16 and 17 (other than C-OH) of the

Art Unit: 1616

steroid, which would assist the skilled artisan in practicing the claimed invention. The skilled artisan, seeking lead compounds for pharmaceutical discovery and treatment of angiogenesis, would be at a loss as to where to begin such discovery in the absence of such data.

5) The breadth of the claims: Claims are drawn to the method of treatment of angiogenesis by hundreds of compounds as in claims 10 and 19, therefore, claims are considered broad.


6) The quantity of experimentation needed: Since the nature of the method is so unpredictable, as can be seen by the prior art cited above and since the claims are drawn to a broad range of pharmaceuticals for treatment of angiogenesis and since there is a lack of guidance present in the specification, the skilled artisan would have to undertake undue experimentation to practice the claimed invention commensurate with the scope of the claims.

Since the significance of particular for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine the activity of all the estradiol analogues have the property of angiogenesis.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Naim Qazi whose telephone number is 703-305-3910. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

November 29, 2002


SABIHA QAZI, PH.D
PRIMARY EXAMINER